

REMARKS

Upon entry of the amendment, claims 1-7, 9-20, and 22-32 will be pending in the application. Claims 8, 21, and 33-35 have been cancelled for being drawn to non-elected subject matter. Claim 1 has been amended to incorporate the subject matter of original claim 2, which is now cancelled. Claim 7 has been amended to correct a typographical error. Support for the amendment to claims 10, 31, and 32 appears in the specification at, e.g., page 12, lines 17-21. Support for the amendment to claim 25 appears in the specification at, e.g., page 7, lines 13-17. New claim 36 is supported in the specification at page 11, lines 12-14. No new matter has been added.

The specification has been amended to insert the serial number of one priority application and to correct the reference to the filing date of a second priority application.

A supplemental information disclosure statement (IDS) accompanies this response. The IDS encloses references that were not initialed by the Examiner in the Form 1449 returned with the Office Action.

Rejections under 35 USC § 112, first paragraph

Claims 1, 3-7, and 9 are rejected for overbreadth. The rejection is traversed to the extent it is applied to the claims as amended.

Claim 1, from which depend claims 3-7, has been amended to incorporate the subject matter of claim 2, which is not subject to the rejection. Independent claim 9 has also been

amended to incorporate the subject matter of claim 2. Accordingly, this rejection can be withdrawn.

Claims 10, 31, and 32 are rejected for overbreadth. The rejection is traversed to the extent it is applied to the claims as amended.

Claims 10, 31, and 32 have been amended to clarify that the claimed method is drawn to a method of inhibiting tissue transplantation associated or blood transfusion-associated graft versus host (GVH) response, or a method of inhibiting a tissue transplantation or blood transfusion-associated alloantibody response in a patient. As such, the claims are no longer drawn to a method preventing the occurrence of GVH or alloantibody response in a patient in any circumstance but instead to inhibiting a response that occurs following a transplantation or transfusion. An example falling within the scope of the claimed invention is provided at page 25, line 16 to page 14 (Example 6). The example shows that treating allogenic donor cells with an ethylene oligomer prior to transplantation inhibits an immune response in an in vivo transfusion-associated GVH model.

In view of the foregoing comments, reconsideration and withdrawal is requested of the rejection for overbreadth.

Rejections under 35 USC § 103(a)

Claims 1-7, 9-20 and 22-32 are rejected as obvious over Drobyski et al., Bone Marrow Transplantation 10:301-04, 1992 ("Drobyski") in view of Budowsky, US Patent No. 6,369,048, ("Budowsky").

Claim 1 (from which depends claims 2-7) and claim 9 are drawn to a method of treating a patient with an immune dysfunction by treating peripheral blood mononuclear cells (PBMC)

with an effective amount of an aziridino-containing compound and then administering the treated cells to the patient.

The Examiner has the initial burden of establishing that the teachings of the applied art would have suggested the claimed invention to one of ordinary skill in the art and that such person would have had reasonable expectation of success. In re O'Farrell, 853 F.2d 894, 904, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). However, this suggestion must be in the prior art and not in the Applicants' disclosure. In re Dow Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

With the instant rejection, the Examiner has improperly relied on Applicants' specification to find motivation for combining the references. Applicants teach in their specification that an immune dysfunction can be treated by treating peripheral blood mononuclear cells (PBMC) with an effective amount of an aziridino-containing compound and then administering the treated cells to the patient. However, motivation for making the claimed invention is absent in the applied art. Neither reference describes or suggests a method in which a PBMC is treated with an aziridino compound in an amount sufficient to inhibit replication of a nucleated cell, and then administered to a patient to treat an immune disorder. Drobyski, as noted by the examiner, is completely silent about using cells that have been treated with an aziridino-containing compound. The reference instead describes leukocyte infusion into a leukemia patient that has relapsed after two failed bone marrow transplants. Following the infusion of leukocytes, the leukemia was reported to go into remission. There is no suggestion in this reference, however, of a method that includes treating one of the recited disorders by contacting the leukocytes of a patient with an aziridino-containing compound. In fact, Drobyski

reports that graft-versus-host (GVH) disease, one of the disorders now recited in claim 1, was observed following leukocyte infusion.

Budowsky fails to overcome the deficiencies of Drobyski. Budowsky is concerned with inactivating viral pathogens that may be present in biological compositions, such as blood or blood products. The reference reports that ethylene oligomer inactivating agents and organic solvents can be used to inactivate viruses. However, there is no suggestion in this reference of a method of treating one of the disorders now recited in claim 1 by treating PBMCs with an effective amount of an ethylene oligomer.

In fact, Budowsky states that “it is desirable to leave the structure and function of valuable constituents, such as red blood cells, platelets, leukocytes, proteins, and polysaccharides, relative unchanged “ (col. 1, line 21-24). The claims, however, require a therapeutically effective amount of the aziridino-containing agent, which is “an amount sufficient to inhibit replication of nucleic acid in a nucleated blood cell, e.g., a leukocyte” (see page 11, lines 3-4). Thus, by teaching that it is desirable to use an agent that leaves nucleated cells intact, Budowsky teaches away from the claimed invention. This reference therefore cannot produce the claimed invention when combined with Drobyski. Rather, the only apparent reason discernible for combining the prior art of record is the Applicant’s disclosure. Thus, the Examiner has engaged in impermissible hindsight to arrive at the conclusion that the claimed invention is obvious over Lopez in view of the ‘975 patent. In re Fritsch, 972 F.2d 1260, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992); W.L. Gore Assocs. v. Garlock, Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-313 (Fed. Cir. 1983) cert. denied 469 U.S. 851 (1984) (“To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the

Applicants: Fast et al.
U.S.S.N. 10/036,768

insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher”).

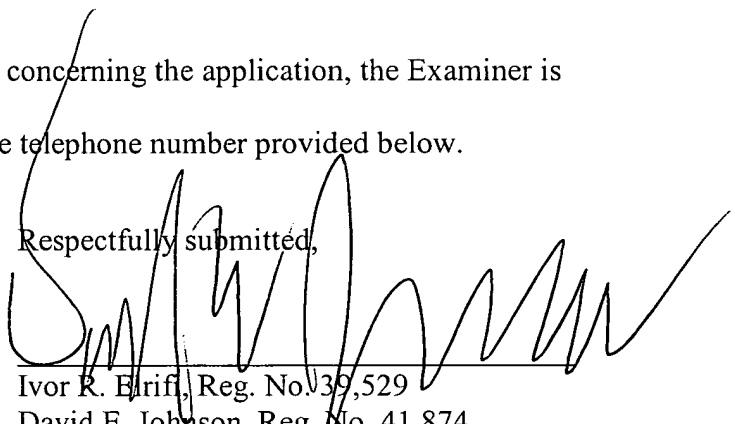
The remaining independent claims subject to the rejection also require a therapeutically effective amount of an aziridino-containing compound (claims 9, 10, and 32) or an ethylene oligomer (independent claims 25 and 31). Therefore, the remaining claims are also non-obvious over the combination over Drobyski and Budowsky.

In view of the foregoing comments, reconsideration and withdrawal of the rejection for obviousness is respectfully requested.

Applicants submit that the application is in condition for allowance and such action is respectfully requested. A petition for extension of time accompanies this response. Please charge any payments or credit any overpayments of the same to Deposit Account No. 50-0311, reference 18242-511.

Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



Dated: January 23, 2004

Ivor R. Briff, Reg. No. 39,529
David E. Johnson, Reg. No. 41,874
Attorneys for Applicants
c/o MINTZ LEVIN
One Financial Center
Boston, Massachusetts 02111
Tel.: (617) 542-6000
Fax: (617) 542-2241